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| 10/723,552 | 11/26/2003 | Jay A. Fishman | 14846-011004 / MGH 0978-2 | 9739 |

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| EXAMINER | |
|---|---|
| CARLSON, KAREN C | |
| ART UNIT | PAPER NUMBER |
| 1656 | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/723,552 | FISHMAN, JAY A. | |
| | Examiner | Art Unit | |
| | Karen Cochrane Carlson, Ph.D. | 1656 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5,8-17,19-22,25 and 26* is/are pending in the application.

4a) Of the above claim(s) *2-5,9-14,19-22 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,15-17 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Art Unit: 1656

**The Notice of Non-responsive Amendment mailed January 16, 2008 is vacated.** The Examiner apologizes for confusing previous Office Actions, resulting in the sending of this Notice to Applicants.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2007 has been entered.

Claims 6, 7, 18, 23, and 24 have been cancelled. Claims 2-5, 9-14, 19-22, and 25 have been withdrawn from further consideration by the Examiner because these claims are drawn to non-elected inventions. Claims 1, 8, 15-17, and 26 are currently under examination.

Priority is set to the filing date of SN 08/766,528, December 13, 1996. The instant SEQ ID NO: 3 is not found in SN 08/572,645 filed December 14, 1995. Rather, '645 teaches instant SEQ ID NO: 1 encoding Tsukuba-1.

**Maintenance of Rejections:**

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 8, 15-17, and 26 are again rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The polypeptide encoded by a nucleic acid comprising the nucleotides 585-2156, 2307-5741, and 5620-7533 of SEQ ID NO: 3 lacks a specific utility. First, these nucleotide regions in SEQ

ID NO: 3 encodes at least 3 different proteins, gag, pol, and env. Review articles in the retroviral art teach that gag is further cleaved into at least matrix (MA), Capsid (CA), and nucleocapsid (NC) (Freed, 2002; J. Virol. 76 (10): 4679-4687; see Fig. 1 for "Generic Gag"). Pol is cleaved into enzymes, and Env cleaved into glycoproteins. In the genome, Gag is further cleaved into p1, p2, and p6. The pol is cleaved into enzymes HIV-1 protease (PR), reverse transcriptase (RT), and integrase (IN), while the env is cleaved into vpu, surface (SU), and transmembrane (TM) envelope proteins (Freed, 1998; Virol. 251:1-15, see Fig. 1A). Besides gag, pol, and env, the HIV-1 genome encodes additional proteins, such as vif, vpr, and nef (Freed, 1998). As in HIV-1, Freed (2002) teaches that gag encodes proteins other than MA, CA, and NC. In mouse leukemia virus (MLV), gag additionally comprises p12; in Rouse sarcoma virus, p2a, p2b, and p10; in Mason-Pfizer monkey virus (M-PMV), p4, p12, and pp24/16; and in equine infectious anemia virus (EIAV), p9. The instant specification is silent as to the function and proteolytic breakdown of polypeptides encoded by the specified regions of SEQ ID NO: 3, having at least 95% identity to the specified regions of SEQ ID NO: 3, or having at least 30 or 100 nucleotides from SEQ ID NO: 3. Indeed, no polypeptides, only deduced amino acid sequences, are taught in the specification.

Additionally, human immunodeficiency virus (HIV-1) proteins result in reduced immune system function, the mouse leukemia virus (MLV) proteins result in leukemia, the Rouse sarcoma virus proteins result in cancer, and the equine infectious anemia virus (EIAV) proteins result in anemia, for example. The instant specification is silent regarding the function of proteins encoded by specified regions of SEQ ID NO: 3, having at least 95% identity to SEQ ID NO: 3, or having at least 30 or 100 nucleotides from SEQ ID NO: 3. Aliyoshi et al. (with inventor Jay Fishman); 1998; J. Virol. 72(5): 4503-4507) teach a retrovirus having 99.9 % identity to SEQ ID NO: 3 (5 mismatches), and encoding the env protein (Fig. 1). Other encoded proteins are not disclosed therein. At page 4503, left col., para. 2, Akiyoshi et al. teach that Type C retroviruses from swine cell lines are known but no disease following infection has been identified.

Therefore, it can be concluded that the polypeptide(s) encoded by specified regions of SEQ ID NO: 3, having at least 95% identity to SEQ ID NO: 3, or having at least 30 or 100 nucleotides from SEQ ID NO: 3 do not have a specific utility.

The polypeptides have not been taught to have a substantial utility, or real world use. While SEQ ID NO: 3 (having at least 95% identity to SEQ ID NO: 3, or having at least 30 or 100 nucleotides from SEQ ID NO: 3) may be a retrovirus, the specification does not teach the function of the encoded proteins. Thus, one skilled in the art would have to carry out further research to identity the use of these encoded polypeptides.

The specification does not assert any utility for the encoded polypeptides; thus, the polypeptides lack credible utility because no utility is offered.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8, 15-17, and 26 are also again rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, credible, or operable, asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

At page 5, para 4, Applicants request clarification of the assertion that no polypeptides or polypeptides sequences are disclosed in the specification. This statement is a carry-over from an earlier Office Action in which the amino acid sequence were lacking from the sequence

listing. For clarification, this assertion has been modified to state that "no polypeptides, only deduced amino acid sequences, are taught in the specification".

At page 6, Applicants urge that Akiyoshi et al. supports a utility for swine retroviral polypeptides for the use of pig-derived tissues for xenotransplantation into humans. Again, the implications of being infected with the virus are not taught in the instant specification or in Akiyoshi. As noted above, at page 4503, left col., para. 2, Akiyoshi et al. teach that Type C retroviruses from swine cell lines are known but no disease following infection has been identified.

At page 6, para. 3, Applicants state that the Examiner has not offered any evidence that SEQ ID NO: 3 is not a retrovirus. The Examiner did not state that SEQ ID NO: 3 was not a retrovirus. Applicants should focus on the phrase "the specification does not teach the function of the encoded proteins".

At page 6, para. 4, of their response, Applicants again urge again that the specification teaches methods and reagents for detecting porcine retroviruses that are useful for screening donor animals to determine infection and as a measure of the appropriate level of immune suppression. Since this method is carried out using the polypeptides claimed, it is not a non-specific utility.

Again, this argument is not persuasive because this is a "reach through" utility, that is, one must make all of the polypeptides encoded by SEQ ID NO: 3, make all of the antibodies specific to these polypeptides, then determine for themselves if the detection of these polypeptides has any bearing on xenograft transfer. It is not for another to arrive at Applicant's invention. As noted, many polypeptides are encoded by SEQ ID NO: 3. Applicants have not provided a function for any of these polypeptides. These polypeptides differ from prostate specific antigen (PSA), for example, where the detection of PSA is an indicator of prostate cancer. Thus, using ELISA to detect the claimed polypeptides is tantamount to isolating the

polypeptide, which is a circular utility. In the instantly claimed invention, the polypeptides are not in hand and no function is provided for these polypeptides One cannot know until they determine for themselves if detection of any one of the polypeptides will be an indication that a donor animal will pass the nucleic acid retroviral vector to the xenograft recipient and cause deleterious effects. Thus, the polypeptides encoded by specific regions of SEQ ID NO: 3 lack a specific utility.

At page 7, para. 2, Applicants argue that the Examiner states that "Since this method is carried out using the polypeptides claimed, it is a non-specific utility", the rejection is not logical. The phrase is correctly written in the last Final Rejection at page 4, last line, as a concluding summary of Applicants arguments: "Since this method is carried out using the polypeptides claimed, it is **not** a non-specific utility".

Applicants discuss "reach through" utility statements at page 7, last paragraph, which is repeated above as the Examiner's argument to another of Applicant's arguments. Applicants argue that the logic underlying the assertion that the claimed polypeptides are useful in the detection of retroviral activation in xenotransplantation is not flawed or inconsistent with logic. Applicants continue to skirt the issue. The issue is, why would one skilled in the art want to assess if a pig carrries this virus and expresses these claimed encoded proteins?? Does the presence of these proteins matter in xenotransplantaion? It is not for another to determine why these proteins should be detected in xenotransplantation. As noted in the previous rejections and above, and again here:

In the instantly claimed invention, **the polypeptides are not in hand and no function is provided for these polypeptides** One cannot know until they determine for themselves if detection of any one of the polypeptides will be an indication that a donor animal will pass the nucleic acid retroviral vector to the xenograft recipient and cause deleterious effects. Thus, the polypeptides encoded by specific regions of SEQ ID NO: 3 lack a specific utility.

Regarding Applictants discussion of ELISA at page 8, para. 1, Applicants do not understand the utility is circular. Again, Applicants do not have the protein in hand and no

function has been assigned to any of the proteins. To find the protein for further research, determining what it does or even if it's detection is of wider use in xenotranplantation, for example, is a circular utility. Again, one would have to make the proteins, antibodies to the proteins, and detect the protein in an animal. This is a reach through utility, in the same order as isolating the protein encoded by a nucleic acid. The proteins are not in hand, and the result of infection is unknown. Therefore, the Examiner disagrees that the ELISA is a utility for the claimed polypeptides.

Applicants again argue (at page 8-9) that the references cited in the rejection prove that the polypeptides claimed have a well-established utility. Again, Applicants appear to be overlooking the point of the citations. The reason why the citations were provided is to show that retroviruses have different functions: "human immunodeficiency virus (HIV-1) proteins result in reduced immune system function, the mouse leukemia virus (MLV) proteins result in leukemia, the Rouse sarcoma virus proteins result in cancer, and the equine infectious anemia virus (EIAV) proteins result in anemia, for example. The instant specification is silent regarding the function of proteins encoded by specified regions of SEQ ID NO: 3, having at least 95% identity to SEQ ID NO: 3, or having at least 30 or 100 nucleotides from SEQ ID NO: 3".

Claims 1, 8, 15-17, and 26 are again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification and claims do not set forth any structure of or function for the claimed polypeptides encoded by specified regions of SEQ ID NO: 3, having at least 95% identity to SEQ

ID NO: 3, or having at least 30 or 100 nucleotides from SEQ ID NO: 3. Also, this polypeptide is not in hand. Therefore, the specification lacks written description for the claimed polypeptide(s).

Applicants urge at page 9 of their response that the determination of polypeptide sequences encoded by a given nucleic acid sequence is well within the capabilities of skilled artisans and that polypeptide sequences are disclosed in Figure 3.

The argument continues to not persuasive because there is no correlation of structure with function. Therefore, one skilled in the art could not determine which polypeptides fall within the claimed invention, that is, polypeptides encoded by a polynucleotide having at least 95% identity to specified regions of SEQ ID NO: 3 may have activities other than full-length polypeptides encoded by SEQ ID NO: 3, which polypeptides have no disclosed functions.

Again, there must be a correlation of structure and of function to meet the written description requirement. The specification does not teach the function of the polypeptides. It is not enough to know that Gag proteins aid in the assembly of viral particles in general. For this retrovirus, what is the function of this Gag protein? If infected, will the pig develop anemia? This is not disclosed in the specification. No function is provided for any of the encoded polypeptides, and Applicants are not in possession of any variants of the encoded polypeptides.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 8, 15-17, and 26 are again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims refer to "A polypeptide..." As noted above in the rejection under 35 USC 101, retroviruses encode many polypeptides; therefore, it is not clear which polyeptide is being claimed.

Claim 1 refers to "95% identical". The term "identical" is an absolute term, meaning that one thing is identical to another or it is not. Thus, one skilled in the art cannot know what a fraction of identical means.

Applicants state that Claim 1 uses the term "identity" which the Examiner has agreed that the term is clear. Claim 1 continues to use the word "identical".

No Claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen Cochrane Carlson, Ph.D./
Primary Examiner, Art Unit 1656